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Fractal analysis of alveolarization in hyperoxia-induced rat models of bronchopulmonary dysplasia

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Many morphometric approaches have been proposed for quantitative evaluation of alveolarization in experimental models of bronchopulmonary dysplasia (BPD), such as alveolar number, alveolar size and variability, mean linear intercept (L_m), surface-to-volume ratio, or radial alveolar count. Conversely, no papers are available about potentiality of fractal analysis in this matter. Thus, in the present study, we performed a comparative analysis between L_m and fractal parameters (fractal dimension (D) and lacunarity (λ)), in experimental hyperoxia-induced models of BPD. At birth the newborn rats were randomly distributed between the following experimental groups: a) rats raised in ambient air for 2 weeks; b) exposed to 60% oxygen for 2 weeks; c) raised in normoxia for 6 weeks; d) exposed to 60% hyperoxia for 2 weeks and then to room air for further 4 weeks.

Normoxic 6-weeks rats showed a significant decrease of L_m and a significant increase of D and λ with respect to normoxic 2-weeks rats, indicative of alveolar development. Hyperoxia-exposed rats of 2 weeks did not show significant changes in L_m and D with respect to normoxic rats equal in age, although λ was significantly lower in hyperoxic group. Conversely, in the comparison between 6-week rats, the hyperoxia-exposed group showed higher value of L_m and lower values of D and λ, when compared to the normoxic group, confirming a lower alveolar gas exchange surface-to-volume ratio and an airspace morphology of lower complexity. The analysis of the ROC curves showed a comparable discriminatory power of L_m and D as binary classifiers of the airspace morphology (areas under the curves of 0.815 and 0.753, respectively). Moreover, the values exhibited by the parameters when different segmentation thresholds were applied suggested that fractal parameters are less sensitive (D and λ showed a coefficient of variation of 0.005 and 0.009, respectively) than L_m (exhibiting a coefficient of variation of 0.05) to the bias eventually introduced in the analysis by approximations or errors in tissue segmentation.

In conclusion, the present study demonstrated the ability of fractal analysis (D and λ) to identify developmental and hyperoxia-induced changes in alveolarization with discriminatory power similar to L_m. The fractal approach, however, appears more fit to automatic image analysis, being less influenced by approximations in thresholding and image editing.

Keywords

Morphometry; Fractal analysis; bronchopulmonary dysplasia.